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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,195	02/04/1999	GEORGE BARRIE KITTO	D6073	3475

27851 7590 09/10/2002

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EXAMINER
PARKIN, JEFFREY S

ART UNIT	PAPER NUMBER
1648	12

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/244,195	KITTO, G. B., AND M. S. BURNET	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, and 5-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

Status of the Claims

1. Acknowledgement is hereby made of receipt and entry of the submission filed 10 June, 2002, wherein claims 1 and 6 were amended. Claims 1-2 and 5-11 are pending in the instant application.

35 U.S.C. § 103(a)

2. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the

time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

4. Claims 1, 2, and 5-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brey *et al.* (1992), in view of Georgiou *et al.* (1994), and further in view of Haseltine *et al.* (1991), Kang (1993), and Rodman (1997). As previously set forth, Brey *et al.* (1992) describe the preparation of S. *typhimurium* expression systems (including those derived from strain SL3261) that are useful for the expression of heterologous (e.g., malaria) antigens. This teaching does not disclose the utilization of an Lpp-OmpA-Tat fusion protein. Georgiou *et al.* (1994) describe the preparation of recombinant DNAs that are suitable for the expression of a heterologous antigen on the external surface of an enteric microorganism (e.g., E. *coli* or Salmonella). DNA constructs were prepared that were capable of encoding fusion proteins comprising the Lpp signal sequence, OmpA coding portion, and a heterologous antigen (i.e., see Figure 1). This teaching does not disclose recombinants expressing the HIV-1 *tat* gene. Haseltine *et al.* (1991), Kang (1993), and Rodman (1997) all provide the complete nucleotide/amino acid sequence of the HIV-1 *tat* gene and expression vectors comprising said gene. These teachings all illustrate the medical importance of Tat.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to express the HIV-1 *tat* gene provided by Haseltine *et al.* (1991), Kang (1993), or Rodman (1997), as an Lpp-OmpA-Tat fusion protein, as suggested by Georgiou *et al.* (1994), in the S. *typhimurium* expression system described by Brey *et al.* (1992), since Brey and colleagues teach that this system is useful for generating strong

immune responses against the antigen of interest. The skilled artisan would have been motivated to prepare such constructs since this would facilitate the development of HIV-1 Tat-specific immunological reagents (i.e., antibodies) which can be employed in diagnostic, immunological, or biochemical assays. It would have also been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare a fusion protein comprising the Lpp signal sequence, OmpA, and HIV-1 Tat since Georgiou *et al.* (1994) teach that Lpp-OmpA-X fusion proteins are expressed in large quantities in an antigenic/immunogenic form on the cell surface of enteric bacteria.

Applicants traverse and submit that the combination of references do not render the claimed invention obvious and that there was no reasonable expectation of success. Applicants' arguments have been carefully considered but are not deemed to be persuasive. As set forth *supra*, all of the components employed by the applicants (e.g., attenuated bacterial host, surface exposure fusion antigen, and viral transactivating protein were well-known in the prior art. Both the bacterial host and fusion protein had already been used to produce recombinant proteins. Moreover, viral transactivating proteins have been cloned, sequenced, and expressed in disparate expression systems. Therefore, there was a reasonable expectation of success of sufficient motivation for combining the aforementioned references.

5. Claims 1, 2, and 5-11[1] are rejected under 35 U.S.C. § 103(a) as

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[1] As previously set forth, the teachings of Hone and colleagues describes the use of an S. *typhimurium* strain carrying a mutation in the *aro* locus. This attenuated bacterial strain appears to be the same strain described by Fouts *et al.* (1995, Construction and immunogenicity of *Salmonella typhimurium* vaccine vectors that express HIV-1 gp120, Vaccine, 13(17):1697-705) which was designated strain SL3261. Since the Patent Office does not have the facilities for examining and comparing applicants' claimed S. *typhimurium*

being obvious over Hone *et al.* (1996) in view of Georgiou *et al.* (1994), and further in view of Haseltine *et al.* (1991), Kang (1993), and Rodman (1997). Hone and colleagues provide attenuated *Salmonella typhimurium* vaccine vectors containing expression vectors encoding *Escherichia coli* OmpA::HIV-1 gp120 fusion proteins. These Salmonella strains induced both mucosal and systemic HIV-1 gp120-specific immune responses. This teaching does not disclose Lpp-OmpA-HIV-1 Tat fusion proteins. Georgiou *et al.* (1994) describe the preparation of recombinant DNAs that are suitable for the expression of a heterologous antigen on the external surface of an enteric microorganism (e.g., E. *coli* or Salmonella). DNA constructs were prepared that were capable of encoding fusion proteins comprising the Lpp signal sequence, OmpA coding portion, and a heterologous antigen (i.e., see Figure 1). This teaching does not disclose recombinants expressing the HIV-1 *tat* gene. Haseltine *et al.* (1991), Kang (1993), and Rodman (1997) all provide the complete nucleotide/amino acid sequence of the HIV-1 *tat* gene and expression vectors comprising said gene. These teachings all illustrate the medical importance of Tat.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to express the HIV-1 *tat* gene provided by Haseltine *et al.* (1991), Kang (1993), or Rodman (1997), as an Lpp-OmpA-Tat fusion protein, as suggested by Georgiou *et al.* (1994), in the S. *typhimurium* expression system described by Hone *et al.* (1996), since Hone and colleagues teach that this system is useful for generating strong immune responses against the antigen of interest. The skilled

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strain SL3261 with the S. *typhimurium* strain employed by Hone *et al.* (1996), the burden is upon applicants to demonstrate the unobvious genotypic/phenotypic differences between the two strains. *In re Best*, 562 F.2d 1252, 195 U.S.P.Q. 430 (C.C.P.A. 1977). *Ex parte Gray*, 10 U.S.P.Q.2d 1922 (Bd. Pat. Appl. Int. 1989).

artisan would have been motivated to prepare such constructs since this would facilitate the development of HIV-1 Tat-specific immunological reagents (i.e., antibodies) which can be employed in diagnostic, immunological, or biochemical assays. It would have also been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare a fusion protein comprising the Lpp signal sequence, OmpA, and HIV-1 Tat since Georgiou *et al.* (1994) teach that Lpp-OmpA-X fusion proteins are expressed in large quantities in an antigenic/immunogenic form on the cell surface of enteric bacteria.

Applicants traverse and submit that the combination of references do not render the claimed invention obvious and that there was no reasonable expectation of success. Applicants' arguments have been carefully considered but are not deemed to be persuasive. As set forth *supra*, all of the components employed by the applicants (e.g., attenuated bacterial host, surface exposure fusion antigen, and viral transactivating protein were well-known in the prior art. Both the bacterial host and fusion protein had already been used to produce recombinant proteins. Moreover, viral transactivating proteins have been cloned, sequenced, and expressed in disparate expression systems. Therefore, there was a reasonable expectation of success of sufficient motivation for combining the aforementioned references.

Finality of Office Action

6. Applicants' amendment necessitated any and all new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS**

FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Correspondence

7. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

8. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

05 September, 2002

James C. Housel 9/9/02

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600